

II. REMARKS

Formal Matters

Claims 42-82 are pending after entry of the amendments set forth herein.

Claims 42-49 and 53-57 examined and were rejected. Claims 50-52 and 58-82 were withdrawn from consideration.

Claims 42, 45, 46, and 49 are amended. The amendments to the claims were made solely in the interest of expediting prosecution, and are not to be construed as an acquiescence to any objection or rejection of any claim. Support for the amendments to claims 42, 45, 46, and 49 is found in the claims as originally filed, and throughout the specification, in particular at the following exemplary locations: the Examples, e.g., page 16, lines 17-20; page 16, lines 22-25; and Figures 3D 4A, 5A, and 6A.

Accordingly, no new matter is added by these amendments.

Please replace claims 42, 45, 46, and 49 with the clean version provided above.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached is captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE.**"

Applicants respectfully request reconsideration of the application in view of the remarks made herein.

Communication dated January 22, 2003

The Communication dated January 22, 2003 stated that the amendment, filed on February 14, 2002 and responsive to the November 20, 2001 Office Action, was not fully responsive because: 1) the amendment did not correct all sequence issues in the claims (claim 49); and 2) the amendment relied upon evidence, copies of which were not of record and were not provided.

Applicants submit that the amendment is now fully responsive. Claim 49 is amended to refer to SEQ ID NO:3. Copies of references referred to in the amendment are provided herewith as Exhibits 1-6. Accordingly, the issues raised in the Communication have been adequately addressed, and the instant amendment is fully responsive to the November 20, 2001 Office Action.

Claim objections

Claims 42-49 and 53-57 were objected to because the claims recite “AT content.” The Office Action stated that Applicant is required to spell the words in the claims.

Without conceding as to the correctness of this rejection, claim 42 is amended to spell out the words adenine and thymine.

Rejection under 35 U.S.C. §112, first paragraph

Claims 42-49 and 53-57 were rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement.

The Office Action stated that: 1) the specification lacks complete deposit information for the deposit of vectors dDS56RBSII, pBi-5, ppTMCS and strains DH5alphaZ1 and FCB-1; and 2) it is not clear that the vectors and strains are known and publicly available or can be reproducibly isolated from nature without undue experimentation. Applicants respectfully traverse the rejection.

The Office Action stated that Applicants have provided a written description of a method for making the claimed vectors and strains, but that this method will not necessarily reproduce vectors and strains which are chemically and structurally identical to those claimed. Applicants note that the claims are directed to methods, not vectors or strains.

The vectors pDS56RBSII, pBi-5, and ppTMCS were publicly available as of the filing date of the instant application, as noted on page 10, lines 9-15 of the instant specification. The specification further notes that other expression vectors can be used. Specification, page 10, lines 14-15. For example, pDS56RBSII was disclosed in Hochuli et al. (1988) *Biotechnol.* 6:1321 (a copy of which is provided herewith as Exhibit 1); and Bujard et al. (1987) *Methods Enzymol.* 155:416 (a copy of which is provided herewith as Exhibit 2). pBi-5 was disclosed in Baron et al. (1995) *Nucleic Acids Res.* 23:3605; (a copy of which is provided herewith as Exhibit 3). The vector ppTMCS is described in Ivana Türbachova, Diploma and Ph.D. Thesis, University of Heidelberg, Germany, 1996/2000 (a copy of the relevant pages of which are provided herewith as Exhibit 4). Exhibit 4 provides a description of the modification of plasmid ppT70/CAT by introduction into ppT70/CAT of a multiple cloning site into NsiI/PacI digested ppT70/CAT. The sequence of the multiple cloning site is provided. The coding region for gp190 was inserted into the multiple cloning site of ppT70/CAT, resulting in the plasmid ppT190, shown in Figure 6 (“Abb. 6: Der ppT190 Vektor”). The ppTMCS plasmid thus includes the

ppT190 vector without the P_{tub-1} promoter, without the SAG-1 3' UTR, and without the gp190 coding sequence.

The bacterial strains used in the methods described in the instant specification are publicly available. For example, *E. coli* DH5αZ1 is described in Lutz et al. (1997) *Nucl. Acids Res.* 25:1203 (a copy of which is provided herewith as Exhibit 5). As of the filing date of the instant application, a wide variety of bacterial strains were available.

The choice of vector or of bacterial strain was not part of the invention. Instead, the invention relates to a method of producing a complete gp190/MSP1 protein comprising expressing a nucleotide sequence encoding the complete gp190/MSP1 protein in a single expression vector.

The FCB-1 strain of *Plasmodium falciparum* is disclosed in Miller et al. (1993) *Molecular Biochemical Parasitology* 59:1 (a copy of which is provided herewith as Exhibit 6).

The Office Action stated that a suitable deposit, evidence of public availability of the vectors and strains, or evidence of reproducibility without undue experimentation is required. Applicants submit that, given the disclosure in the specification, the instant methods as claimed can be readily practiced without undue experimentation. Applicants submit that deposit of the aforementioned vectors and strains is not necessary for one of ordinary skill in the art to practice the invention without undue experimentation.

Applicants submit that the rejection of claims 42-49 and 53-57 under 35 U.S.C. §112, first paragraph, has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

Rejection under 35 U.S.C. §102/103

Claims 42-49 and 53-57 were rejected under 35 U.S.C. §102(b) or §103 as allegedly unpatentable over Holder et al. ((1985) *Nature* 317:270-273; hereinafter "Holder").

The Office Action stated that: (1) Holder discloses a method of producing the gp190/MSP1 protein of *Plasmodium*; (2) although Holder does not state that the AT content of the expressed nucleotide sequence encoding the gp190/MSP1 protein is less than that of a naturally occurring

nucleotide sequence, the overall structure and function of the protein is being viewed as the same; and
(3) the burden is on the applicant to show a non-obvious distinction between the material structural and functional characteristics of the claimed product and the product of the prior art. Applicants respectfully traverse the rejection.

The instant invention differs from Holder in several respects. These differences include the following:

- 1) Holder does not disclose a method of producing the gp190/MSP1 protein of a *Plasmodium*. Holder states that fragments of the P195 gene were expressed as fusion proteins from the cDNA clones described in Holder, and that these fusion proteins had molecular weights of 135K, 105K, 85K and 65K. Holder, page 271, column 2, first paragraph; and page 273, Figure 3. Thus, Holder does not disclose a method for the production of gp190/MSP1.
- 2) Holder does not disclose a method of producing the gp190/MSP1 protein of a *Plasmodium*, comprising expressing a nucleotide sequence encoding the complete gp190/MSP1 protein in a single expression vector. Instead, Holder shows that multiple cDNA clones (designated 1026, 1013, 1017, 1028, 1032, 1007, and G1) were obtained, each of which included only part of the coding region gp190/MSP1 protein. Holder, page 271, Figure 1A. Thus, Holder does not disclose a method for producing gp190/MSP1 comprising expressing a gp190/MSP1 coding sequence in a single expression vector.
- 3) Holder does not disclose a method of producing the gp190/MSP1 protein of a *Plasmodium*, comprising expressing a nucleotide sequence encoding the complete gp190/MSP1 protein in a single expression vector, wherein the AT content of the sequence encoding the gp190/MSP1 protein is less than that of a naturally-occurring sequence. The cDNA clones of Holder were from a naturally-occurring *Plasmodium*. The DNA sequence encoding the gp190/MSP1 was not altered to reduce the AT content. Holder states that the A+T content of the genomic sequence was high, with an average of 76% within the coding region. Holder, page 270, column 1, second paragraph. Thus, Holder does not disclose a method of producing gp190/MSP1 comprising use of a coding sequence for gp190/MSP1 with a reduced AT content compared to naturally-occurring gp190/MSP1.

In view of the differences discussed above, Holder cannot anticipate claims 42-49 and 53-57.

Holder does not render claims 42-49 and 53-57 obvious, as there is no mention in Holder of a method for producing gp190/MSP1 at all, much less a method of producing gp190/MSP1, comprising expressing a nucleotide sequence encoding gp190/MSP1 in a single expression vector. As stated in the specification, until the instant invention, there was not any successful cloning of the whole coding region for gp190/MSP1. Holder does not disclose a method for solving this problem, nor does Holder suggest any such method. Accordingly, Holder cannot render the instant method as claimed obvious.

Applicants submit that the rejection of claims 42-49 and 53-57 under 35 U.S.C. §102(b) or 103 has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.


III. CONCLUSION

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number GRUE003.

Respectfully submitted,
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